CLINICAL PROFILE AND OUTCOME OF ELECTROLYTE DISTURBANCES IN CHILDREN AGED 1 MONTH TO 12 YEARS TREATED IN PAEDIATRIC INTENSIVE CARE UNIT OF A TERTIARY CARE HOSPITAL

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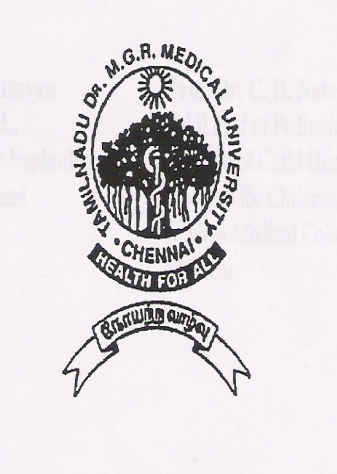

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CERTIFICATE

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CONTENTS

INTRODUCTION

Medical practice rests on the foundation of science. Clinicians are constantly making practical decisions and dealing with situations that demand quick and efficient solutions. The extra ordinary complex functions of the human being depend on the narrow range of the volume and composition of body fluids and electrolytes. These electrolytes run the life with help of meticulously regulated control mechanisms that strictly maintain their levels both extracellularly and intracellularly. There exists a dynamic equilibrium between inflow of water, inorganic substances (i.e., electrolytes) and organic molecules; their distribution between body water compartments and the near-equal outflow of these substances[1].

In an intensive care setting the management of various electrolyte imbalances forms a vital part in life supportive care, more so in paediatric age group. Dyselectrolytemias are commonly encountered in PICU. They do not always manifest specific symptoms but often share the clinical features of underlying illnesses necessitating high index of suspicion. They can be either a primary or secondary co-morbid condition.

TOTAL BODY WATER

Knowledge regarding total body water and distribution of fluids in various body compartments is essential in identification and management of various electrolyte disturbances. Total body water as a percentage of body weight varies with age. From very high TBW in fetus, it gradually decreases to 75% of birth weight in term infants, 60% at 1 year, 60% of body weight in average built adolescent boy and 50% in adolescent girl[2]. TBW is further divided into two main compartments, extra cellular fluid (ECF) and intra cellular fluid (ICF) (Fig.1).

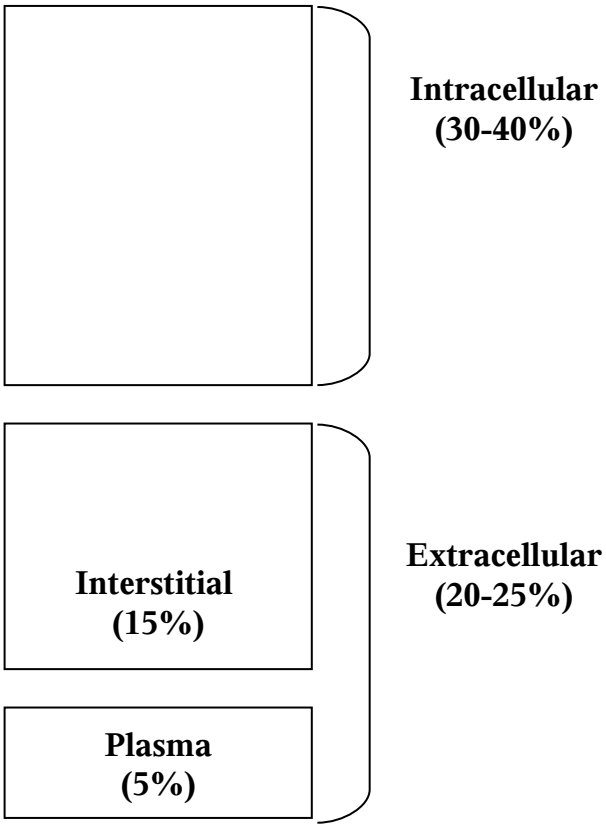

Figure 1: Compartments of body water,expressed as a percentage of body weight[2]

EXTRACELLULAR FLUID (ECF)

The extracellular fluid consists of about one third of total body water. In fetus ECF volume is larger than ICF volume and ECF decreases with age. The ECF is further divided into plasma volume (intravascular) and interstitial fluid (extravascular). Sodium is the principal cation in the ECF and chloride and bicarbonate the principal anions. Under normal circumstances the effective circulating blood volume varies directly with the ECF volume, that is, both increase with sodium loading and decrease with significant salt loss[1] (Fig.2).

INTRACELLULAR FLUID (ICF)

The intracellular fluid compartment consists of fluid inside the cells of the body. It is estimated as the difference between total body water and the ECF compartment. The principal cation in the cells is potassium and the principal anions are phosphates and proteins. The entirely different chemical composition of the ECF and ICF spaces severely limits cation or anion movements in response to tonicity changes in the ECF so that it is the movement of water between ECF and ICF that is largely responsible for the achievement of osmotic equilibrium[1].

PLASMA OSMOLALITY

The plasma osmolality is determined by sodium salts, with lesser contribution from glucose and urea. The plasma osmolality is normally 285-295 mosm/kg.

Plasma osmolality = $2 \times [Na] + [glucose]/18 + [BUN] /2.8$

SODIUM

Sodium is the principal determinant of extracellular osmolality and it is necessary for the maintenance of intra vascular volume. More than 40% of total body sodium is in bone, < 3% of sodium is Intracellular; the remainder in the interstitial and intravascular spaces. Sodium regulation is unique because water balance, not sodium balance, usually determines its concentration. Kidney is the principal site of sodium excretion and is regulated by effective plasma volume not by the plasma osmolality.

HYPONATREMIA

Hyponatremia is defined as serum sodium (Na^+) concentration of less than 135 mEq/L. Whereas hypernatremia always denotes hypertonicity, hyponatremia can be associated with low, normal, or high tonicity. Hyponatremia is the most common electrolyte abnormality encountered in clinical practice, with an incidence of 1.5% of all pediatric hospital admissions[3]. Hyponatremia has also been observed in approximately 30% of patients treated in the intensive care unit[4].

The severity of symptoms is often dependent on the magnitude and rapidity at which serum Na levels decrease from baseline[3]. Symptoms are not correlated with specific serum Na levels. However, they most frequently occur when the serum Na concentration is less than 125 mEq/L. Although morbidity varies widely in severity, serious complications can arise from the disorder itself or during treatment. Understanding the pathophysiology and treatment options is important because the morbidity and mortality of untreated hyponatremia are clinically significant.

PATHOPHYSIOLOGY OF HYPONATREMIA

Hyponatremia can develop because of (1) excessive free water, which mostly happens in hospitalized patients; (2) excessive renal or extrarenal loss of Na; or, in rare cases, (3) deficient intake of Na.

Under normal circumstances, the human body is able to maintain serum Na in normal range (135-145 mEq/L) despite wide fluctuations in fluid intake. The body's defense against developing hyponatremia is the kidney's ability to generate dilute urine and excrete free water[3]. Whenever the ability of the kidney to concentrate urine is affected or overwhelmed, hyponatremia develops.

Deficient intake rarely causes hyponatremia. In children, the most common cause of hyponatremia is loss of Na from the GI tract. Diarrhea is responsible for most incidents of hyponatremia in children. Na loss also occurs in the kidneys. Diuretics are

the most common culprit, followed by other causes, such as salt-losing nephritis, mineralocorticoid deficiency, and cerebral salt-wasting syndrome (CSWS).

Excessive antidiuretic hormone (ADH) secretion causes water retention and subsequent dilutional hyponatremia. ADH is secreted from supraoptic nuclei in response to hyperosmolality and hypovolemia. Secretion of ADH also occurs in response to pain, nausea, vomiting, and morphine intake in postoperative patients. In certain clinical conditions, ADH secretion occurs without any physiologic stimuli, hence the term syndrome of inappropriate ADH secretion (SIADH). In patients with cirrhosis, cardiac failure, or renal failure, hyponatremia may be caused by mechanisms, such as water retention, diuretic use, and decreased Na intake (Fig.3).

Clinical manifestations vary from an asymptomatic state to severe neurologic dysfunction. CNS symptoms predominate in hyponatremia, though cardiovascular and musculoskeletal findings may be present[3]. Factors that contribute to CNS symptoms are (1) the rate at which serum Na levels change, (2) the serum Na level, (3) the duration of the abnormal serum Na level, (4) the presence of risk factors, and the presence of excessive ADH levels.

CNS EFFECTS OF HYPONATREMIA

When serum Na declines, the decrease in serum osmolality results in an osmotic gradient across the blood-brain barrier that causes water to move into the brain

intracellular space. The resultant edema is responsible for symptoms such as apathy, anorexia, headache, nausea, vomiting, irritability, agitation, altered consciousness, seizures and coma[3].

Cerebral adaptation to hyponatremia is accomplished by means of 2 mechanisms: (1) loss of interstitial fluid into the CSF and (2) loss of cellular solute and organic osmolytes.

ACUTE HYPONATREMIA

Patients with acute hyponatremia (developing over 48 h or less) are subject to more severe degrees of cerebral edema for a given serum sodium level. The primary cause of morbidity and death is brainstem herniation[5,6] and mechanical compression of vital midbrain structures. Rapid identification and correction of serum sodium level is necessary in patients with severe acute hyponatremia to avert brainstem herniation and death.

CHRONIC HYPONATREMIA

Patients with chronic hyponatremia (developing over more than 48 h) experience milder degrees of cerebral edema for a given serum sodium level. Brainstem herniation has not been observed. The principal causes of morbidity and death are status epilepticus (when chronic hyponatremia reaches levels of 110 mEq/L or less) and cerebral pontine myelinolysis (an unusual demyelination syndrome that occurs in association with

chronic hyponatremia usually during correction).

Formula for estimating sodium deficit mEq sodium required=(desired[Na] – present[Na])×0.6×weight(kg)

MANAGEMENT OF SYMPTOMATIC HYPONATREMIA

(a) In hypovolemic hyponatremia, the immediate goal is to correct volume depletion with normal NaCl solution. As soon as the patient's blood pressure becomes normal, hyponatremia should be corrected. In patients with seizure, 3% NaCl should be given while volume depletion is corrected.

(b) No consensus has been reached about the optimal treatment of symptomatic hyponatremia. Physiologic considerations indicate that a relatively small increase in the serum Na concentration, on the order of 5%, should substantially reduce cerebral edema. The available evidence indicates that even a 9-mEq/L increase in serum Na concentration over 24 hours can result in demyelinating lesions. Given the risk of demyelinating lesions, the recommended rate of correction should not exceed 8 mEq/L per day[7]. Even hyponatremia-induced seizures can be stopped with mean changes in serum Na of only 3-7 mEq/L.

(c) Treatment of normovolemic hyponatremia due to SIADH requires the administration of 3% NaCl, fluid restriction, and IV administration of furosemide. Furosemide is given to offset the volume expansion created by the 3% Na

infusion. As previously discussed, the plan is to raise the serum Na concentration by 3-7 mEq/L to stop symptoms. Then closely monitor electrolyte levels so that the correction does not exceed 8 mEq/L/day.

(d) In patients with hypervolemic hyponatremia, administer 3% NaCl to stop the symptoms, as previously discussed, and treat the cause.

MANAGEMENT OF ASYMPTOMATIC HYPONATREMIA

(a) In individuals with hypovolemic hyponatremia, the clinical should not rush to correct hyponatremia. The main principle is to avoid hypotonic fluids and to slowly correct Na levels, especially when hyponatremia has been present for 48 hours or longer. When the duration of hyponatremia is unknown, hyponatremia in outpatients, treat as chronic hyponatremia (>48 hours). Closely monitor electrolyte values, and the rate of correction should not exceed 8 mEq/L/d.

(b) In patients with normovolemic hyponatremia, restriction of fluids to two-thirds (or less) of the volume needed for maintenance is the mainstay of treatment. Diuretics can be administered with fluid restriction to remove free water. Once again, the change in Na levels should not exceed 8 mEq/L/d. Avoid hypotonic fluids. Demeclocycline can be used in recalcitrant euvolemic hyponatremia.

(c) In patients with hypervolemic hyponatremia, restrict fluids, and treat the underlying cause.

HYPERNATREMIA

Hypernatremia is defined as a serum sodium concentration >145 mEq/L[2]. It is characterized by a deficit of total body water (TBW) relative to total body sodium levels due to either loss of free water, or infrequently, the administration of hypertonic sodium solutions. In healthy subjects, the body's 2 main defense mechanisms against hypernatremia are thirst and the stimulation of vasopressin release[8].

PATHOPHYSIOLOGY OF HYPERNATREMIA

Hypernatremia represents a deficit of water in relation to the body's sodium stores, which can result from a net water loss or a hypertonic sodium gain. Net water loss accounts for most cases of hypernatremia. Hypertonic sodium gain usually results from clinical interventions or accidental sodium loading. As a result of increased extracellular sodium concentration, plasma tonicity increases. This increase in tonicity induces the movement of water across cell membranes, causing cellular dehydration.

Sustained hypernatremia can occur only when thirst or access to water is impaired. Therefore, the groups at highest risk are infants and intubated patients. Because of certain physiologic characteristics, infants are predisposed to dehydration. They have a large surface area in relation to their height or weight compared with adults, and they have relatively large evaporative water losses. In infants, hypernatremia usually

results from diarrhea and sometimes from improperly prepared infant formula or inadequate mother-infant interaction during breastfeeding[9].

CNS effects of hypernatremia

Hypernatremia causes decreased cellular volume as a result of water efflux from the cells to maintain equal osmolality inside and outside the cell. Brain cells are especially vulnerable to complications resulting from cell contraction. Severe hypernatremic dehydration induces brain shrinkage, which can tear cerebral blood vessels, leading to cerebral hemorrhage, seizures, paralysis, and encephalopathy[10].In patients with prolonged hypernatremia, rapid rehydration with hypotonic fluids may cause cerebral edema, which can lead to coma, convulsions, and death.

Causes of hypernatremia

Sodium excess

* Improperly mixed formula or rehydration solution
    * Excess sodium bicarbonate
    * Ingestion of sea water (480 meq/l)
    * Intentional salt poisoning
    * I.V. hypertonic saline

* Hyperaldosteronism

Water deficit

* Diabetes insipidus – central and nephrogenic
* Diabetes mellitus
* Excessive sweating
* Increased insensible water loss (e.g. newborn on radiant warmer)
* Inadequate access to water
* Lack of thirst

Water deficit in excess of sodium deficit

* Diarrhea
* Osmotic diuretics
* Diabetes mellitus
* Obstructive uropathy
* Renal dysplasia

CLINICAL SIGNS OF HYPERNATREMIA

Doughy feel of skin of the abdomen is pinched, irritability, lethargy, hypertonia, coma, seizures and associated hypocalcemia & hyperglycemia[8].

Treatment of hypernatremia

Initial emergency measures- stabilisation of airway, support of ventilation, if needed, correction of shock with normal saline[2] (Ringer Lactate is not preferred because of its relative hypotonicity) irrespective of serum sodium level and control of seizures. Fluid deficit should be first calculated by estimating dehydration. Fluid to be administrated during 48 hours is fluid deficit plus maintenance plus ongoing losses. Sodium to be given 80 to 100 mEq/L.

* In correcting hypernatremia, do not rapidly decrease the sodium level because a rapid decline in the serum sodium concentration can cause cerebral edema.

* Dehydration should be corrected over 48-72 hours.

* Hypotonicity of fluids is less important the rate of correction.

* The recommended rate of sodium correction is 0.5 mEq/h or up to 10-12 mEq/L in 24 hours[2].

* Once the child is urinating, add 40 mEq/L KCl to fluids to aid water absorption into cells.

In cases of associated hyperglycemia, 2.5% dextrose solution may be given. Insulin treatment is not recommended because the acute decrease in glucose, which

lowers plasma osmolality, may precipitate cerebral edema. Calcium may be added, if the patient has an associated low serum calcium level.

In acute hypernatremia, correction of serum sodium can be achieved rapidly because idiogenic osmoles will not be present in brain cells. Whenever the duration of the hypernatremia is unclear,slow correction is recommended[8]. If the serum sodium concentration is > 200 mEq/L, dialysis should be done by using a high-glucose, low-sodium dialysate.

POTASSIUM

Potassium is the most abundant intracellular cation and is necessary for maintaining a normal charge difference between intracellular and extracellular environments. The intracellular concentration is 150mEq/L is much higher than the plasma concentration. Potassium homeostasis is integral to normal cellular function and is tightly regulated by specific ion-exchange pumps, primarily by cellular, membrane-bound, sodium-potassium adenosine triphosphatase (ATPase) pumps. Majority of body potassium is contained in muscle. The majotity of extracellular potassium is in bone; less than 1% in plasma. Derangements of potassium regulation often lead to neuromuscular, gastrointestinal, and cardiac conduction abnormalities. Kidney is the principal site of excretion.

Hypokalemia

Hypokalemia, a commonly encountered electrolyte disturbance, has diverse as well as serious manifestations like muscular paralysis, paralytic ileus, respiratory muscle paralysis, cardiac arrhythmia and even arrest. Hypokalemia has clinically diverse manifestatons and at times can even mimic diseases like acute poliomyelitis and post diphtheritic paralysis. Potassium deficit usually affects the excitability of nerve and muscles and contractility of skeletal, smooth and cardiac muscles. Hypokalemia is more likely to develop in malnourished children due to pre-existing potassium depletion[11]. Hypokalemia was defined as serum potassium less than 3.5 mEq/L[12]. The hypokalemia was graded as mild (3-3.4 meq/L), moderate (2-2.9 meq/L) and severe (<2 meq/L)[13].

Hypokalemic states[14]

Excessive renal losses

* Tubular diseases(eg.,drugs,cystinosis)
* Steroids (e.g.,aldosterone, glucocorticoids)
* Diuretics
* Non reabsorbable anions (e.g., pencillins, bicarbonate)
* Hypomagnesemia

Non renal losses

* Vomiting
* Diarrhea
* Laxative abuse

Shift from extracellular to intracellular fluid

* Insulin
* β-2 catecholamines
* Alkalosis
* Limited Intake

ECG changes in Hypokalemia

Flattened T wave, depressed ST segment, appearance of U wave and arrhythmias.

Treatment of hypokalemia

Mild hypokalemia (3.0 -3.5 mEq/L) – potassium rich diet, oral potassium supplements 2 meq/kg/day.

For moderate (2.0 -3.0 mEq/L) and severe (<2.0 mEq/L) potassium concentration of maintenance fluid is increased to 40 mEq/L. Rate of infusion should be <0.3 mEq /kg/ hour. For life threatening complications intravenous potassium 0.5-1 meq/kg over 1 hour can be infused through central venous catheter and under continuous ECG monitoring[2].

Hyperkalemia

Hyperkalemia is a potentially life-threatening illness that can be difficult to diagnose because of a paucity of distinctive signs and symptoms. Hyperkalemia is defined as a potassium level greater than 5.0 mEq/L[2].

Ranges are as follows:

* 5.0-6.0 mEq/L - Mild
* 6.1-7.0 mEq/L - Moderate
* 7.0 mEq/L and greater - Severe

Cut-off value is higher in neonates and infants. The major consequences of hyperkalemia result from its neuro muscular effects and life threatening arrythmias.

Pathogenesis of hyperkalemia[14]

Altered renal excretion

* Oliguria
* Chronic hydronephrosis
* Potassium sparing agents
* Impaired external regulation
* Diabetes mellitus
* Adrenal insufficiency

* Drugs (β blockers, ACE inhibitors, heparin)

Shift from intra cellular to extra cellular fluid

* Rapid cell break down (e.g.trauma,cancer chemotherapy)
* Acidosis
* Hypertonicity
* Succinyl choline

Increased intake

* Intra venous solutions
* Potassium containing salt substitutes

Spurious hyperkalemia

* Thrombocytosis (>500,000 mm^3)[15]
* Difficult blood drawing (hemolysis)

ECG changes of hyperkalemia

An ECG is essential in all children in whom hyperkalemia is suspected. ECG reveals the sequence of changes as follows:

* Serum K^+ 5.5- 6.5 mEq/L - Tall, peaked T waves with narrow base, best seen in precordial leads.
* Serum K^+ 6.5- 8.0 mEq/L - Peaked T waves, prolonged PR interval, decreased or disappearing P wave, widening of QRS, amplified R wave.

* Serum K^+ greater than 8.0 mEq/L - absence of P wave, progressive QRS widening, intraventricular /fascicular /bundle branch blocks, progressive widening of QRS, eventually merging with the T wave just before cardiac arrest, forming the Sine-wave pattern .

Treatment of Hyperkalemia

Hyperkalemia is a true medical emergency, with 3 primary goals of immediate management:

(1) Stabilizing the myocardial cell membrane to prevent lethal cardiac arrhythmia (and to gain time to shift potassium intracellularly and enhance potassium elimination).

* Calcium chloride IV

* Calcium gluconate IV

(2) Shifting potassium intracellularly

* Sodium bicarbonate IV

* Regular Insulin and glucose IV

* Inhaled beta-adrenergic agents, such as albuterol (used to manage hyperkalemia with variable results).

(3) Enhancing total body potassium elimination

* Sodium Polystyrene Sulfonate PO/PR or Kayexelate

* Furosemide (only if renal function is maintained)

* Emergent hemodialysis.

Calcium

Calcium is a divalent cation that plays an important role in maintaining membrane potential and in various intracellular enzyme processes. 99% of body calcium is in bone, mostly as hydroxyapatite. Two principal goals of calcium homeostasis- first, adequate net intake of calcium to permit normal skeletal growth and mineralization, second, tight regulation of the serum calcium to permit normal physiologic functioning. Second goal takes precedence over the first goal; skeletal mineralization may be sacrificed to maintain a normal calcium level[16].

Though total calcium provides a satisfactory assessment of physiologic calcium, the level of ionized calcium is more relevant. Differences occur in the presence of hypoalbuminemia and acid base disturbances, commonly encountered in critically ill children[17].

Hypocalcemia

Hypocalcemia is defined as total calcium < 8.8 mg/dl or ionized calcium < 1.12 mmol/l[16]. Cut off values are lower in immediate new born period.

Causes of hypocalcemia[18]

Hypocalcemia in infants and children

Vitamin D deficiency, Hypoalbuminemia, Hypoparathyroidism, Renal failure, Alkalosis, Malabsorption syndrome, Pancreatitis, Hungry bone syndrome, Hypophosphatasia, Hypomagnesemia , Septicemia and septic shock[19] and Critically ill children.

Clinical features of hypocalcemia

Symptoms are mostly due to neuro muscular irritability. Mild hypocalcemia is usually asymptomatic. Acute onset hypocalcemia may present with lethargy, poor feeding, vomiting, abdominal distension, tetany, seizures, cramps, stridor due to laryngo spasm or apnea. Long standing cases show skeletal deformities in addition. ECG may show a prolonged QTc interval.

Treatment of hypocalcemia

For critically ill patients with hypocalcemia intravenous therapy is indicated in the form of 10% calcium gluconate in a dose of 1-2 ml/kg iv over 3 to 5 min with cardiac monitoring .The short treatment is followed by 100-200 mg/kg/day , switched over to oral calcium supplements after recovery from acute illness.

Hypercalcemia

Hypercalcemia is defined as total calcium > 10.8mg/dl or ionized calcium >1.23 mol/l. Hypercalcemia is conventionally classified as mild (< 12 mg/dl), moderate

(12-15mg/dl) or severe (>15 mg/dl)[16].

Causes[18]

Hypercalcemia in infants-- Subcutaneous fat necrosis, Vitamin D excess, Idiopathic infantile Hypercalcemia, Williams syndrome, Blue diaper syndrome, Severe autosomal recessive hyperphosphatasia

In older children-Vitamin D Excess, Primary hyperparathyroidism, Immobilization, Milk alkali syndrome, Thiazide diuretics.

Clinical features of Hypercalcemia

Poor feeding, emesis, failure to thrive, abdominal pain, pancreatitis, hypertension, arrythmias, lethargy, hypotonia, psychiatric disturbances, coma, polyuria, dehydration, hypernatremia, renal failure, nephrolithiasis.

Treatment of Hypercalcemia

Correct dehydration, saline diuresis with loop diuretics, glucocorticoids calcitonin and rarely bisphosphonates.

ACID BASE DISTURBANCES

METABOLIC ACIDOSIS

Metabolic acidosis occurs frequently in hospitalized children; diarrhea is the common etiology. Presence of metabolic acidosis helps narrowing differential diagnosis. Three basic mechanisms for various etiologies are[2] (1) loss of bicarbonate from the body, (2) impaired ability to excrete acid by the kidney and (3) addition of acid to the body (exogenous or endogenous).

Causes of Metabolic Acidosis

Normal anion gap- Diarrhea, renal tubular acidosis, urinary tract diversions, post hypocapnia and ammonium chloride intake.

Increased anion gap- Lactic acidosis (due to various etiologies), ketoacidosis, renal failure, poisonings and IEM.

Clinical features of Metabolic Acidosis

Manifest with features of primary illness and acidotic breathing. At serum pH <7.20 there is impaired cardiac contractility and increased risk of arrythmias. Decrease the cardiovascular response to catecholamines[2]. Severe acidemia impairs brain metabolism, eventually resulting in lethargy and coma.

Treatment of metabolic acidosis

Treatment of underlying disorder, if possible (i.e.,insulin in DKA, base therapy in renal failure, RTA and IEM, adequate perfusion in lactic acidosis)

Dialysis in refractory, severe acidosis.

Specific treatment in toxin ingestion and adrenal insufficiency.

REVIEW OF LITERATURE

Subba Rao *et al* studied the frequency of electrolyte imbalance at admission and their impact on morbidity and mortality in children admitted to a PICU. 305 children admitted over a period of 18 months were studied prospectively for disturbances of sodium and potassium. 32.45% were found to have electrolyte abnormalities. Hyperkalemia was the commonest found in 14.4% cases followed by hyponatremia in 9.5% of children.mortality among children with dyselectrolyemias was 24.2%. Mean duration of hospital stay was found to be significantly prolonged in children with hyperkalemia and hyponatremia. Risk of mortality was also higher in children with dyselectrolytemias[20].

A retrospective analysis of the case records of 290 children admitted to the PICU over a period of one year by Singhi *et al* , studied the frequency ,severity, risk factors and mortality of hypokalemia and efficacy of therapy used for its correction. 14.8% patients were found to have hypokalemia. Predisposing factors included the nature of primary disease (renal disease 19%, septicemia 19%, acute diarrhea 14%, heart disease with CCF 12% and meningoencephalitis 12%), malnutrition and therapy with drugs (diuretics, corticosteroids and antiasthma drugs). The overall mortality among patients with hypokalemia (25%) was significantly higher than among the remaining PICU patients (10.9%)[21].

In a prospective study of 727 acutely ill children upto 12 years of age who

attended the Paediatric Emergency Services done by Singhi *et al*, hypokalemia was found in 13.9% and hyperkalemia in 5.4% of children. 51.48% of hypokalemic children had associated hyponatremia. Patients with hypokalemia had significantly higher risk of mortality as compared to normokalemic children. A significant increase in the mortality was seen with worsening of hypokalemia[22].

A prospective cross-sectional study by Thomas *et al* was conducted in a referral teaching hospital in South India. 143 patients with hyperkalemia (>5 mEq/L) were selected and evaluated. The study concluded that hyperkalemia was twice as common in males. Potassium supplementation and drugs were the leading predisposing causes for hyperkalemia, with renal failure coming distant second. Hyperkalemia developed after admission to hospital in more than 75% of patients[23].

A prospective study by Prasad *et al* evaluated the frequency, clinical characteristics and causes of hyponatremia in 727 patients less than 12 years of age requiring hospitalization. Hyponatremia was found in 29.8% and was frequent in summer (36%). Acute lower respiratory infections (pneumonia) and acute diarrhea each accounted for 20% of cases. Concurrent plasma and urine osmolality evaluation suggested that hyponatremia associated with pneumonia, meningitis, septicemia and seizures were of hypotonic-euvolemic type and in acute diarrhea –hypovolemic type. The study has shown that hyponatremia occurs frequently in sick children requiring emergency care, especially in summer months and should receive appropriate

attention[24].

1330 children under 3 years of age admitted to general ward of ICDDR for diarrhea with complications were studied retrospectively by Samadi *et al* for the relation between types of dehydration, age and nutritional state. 20.8% were hyponatremic, 72.8% isonatremic and 6.5% hypernatremic. The incidence of hyponatremia increased with age. There was a strong relation between types of dehydration and nutritional state. The mortality was 10% for hyponatremia, 4% for isonatremia and 12% for hypernatremia[25].

A prospective study of bacterial meningitis in children was conducted by Kaplan *et al*., serum sodium concentrations below 135 mEq/L were noted in 58% of patients admitted to the study. Low initial serum sodium concentration and prolonged depression in serum sodium despite fluid restriction correlated significantly with the presence of neurologic sequlae of the disease[26].

Singhi et al studied the association between hyponatremia (serum sodium <130 mEq/L) and the final outcome of illness. They correlated serum sodium concentration with the length of hospital stay and mortality in a prospective study of 727 sick children. The mean duration of hospital stay was significantly prolonged in hyponatremic children as compared to children with normal serum sodium levels. The mortality rate among children with severe hyponatremia was 17%, significantly higher than that among normonatremic children who had a mortality of 5.3%. They concluded that

hyponatremia in acutely ill children at admission indicates a poor prognosis[27].

Moritz *et al* studied the changing pattern of hypernatremia in hospitalized children. They reviewed the medical records of 68 children with serum sodium > 150 mEq/L admitted to a large urban children's hospital. The etiologies, predisposing factors, morbidity and mortality associated with hypernatremia were evaluated. The primary factors that contributed to hypernatremia were inadequate fluid intake 76%, followed by gastrointestinal losses 44%, high urinary water losses 44% and sodium excess in 26%. Associated neurologic impairment was found in 38% of hypernatremic children. They concluded that hypernatremia was primarily a hospital acquired disease, produced by the failure to administer sufficient free water to patients unable to care for themselves. Failure to correct hypernatremia increases the risk of mortality[28].

A retrospective study done in neurological/neurosurgical intensive care units by Aiyagari *et al* showed that hypernatremic patients had a lower median admission Glasgow Coma Scale score (8 vs 14, $P < .001$), higher initial Acute Physiology and Chronic Health Evaluation II probability of death (34.9% vs 19.1%, $P < .001$), higher incidence of mechanical ventilation (80.5% vs 41.1.5%, $P < .001$), higher mortality (30.1% vs 10.2%, $P < .001$), and higher incidence of renal failure (10.3% vs 0.9%, $P < .001$). Mortality increased with increasing hypernatremia; however, only severe hypernatremia (serum sodium >160 mEq/L) was independently associated with increased mortality[29].

Cardenas-Rivero *et al* prospectively studied the prevalence and clinical consequences of hypocalcemia in 145 paediatric intensive care unit patients. The prevalence of ionized hypocalcemia was 17.9% (26/145). Death occurred in 8 (31%) of 26 patients with ionized hypocalcemia versus 3 (2.5%) of 119 patients with normocalcemia (p less than 0.0001). More of the children with ionized hypocalcemia had sepsis (p = 0.0299) and they required the administration of vasopressor agents more often (p = 0.0002) than their normocalcemic counterparts. They concluded that ionized hypocalcemia was common in severely ill children and was associated with higher mortality rate[30].

Singhi *et al* studied the incidence of hypocalcaemia in critically ill children admitted to a Paediatric Intensive Care Unit (PICU) and its correlation with outcome. Hypocalcaemia was present in 35 per cent of patients at admission and occurred in another 13 per cent during hospital stay. The incidence of hypocalcaemia (serum total calcium < 8.5 mg/dl) was 22.4, and ionized hypocalcaemia (serum ionized calcium < 3.2 mg/dl) was 32.4 episodes/100 patient days. Mortality was significantly higher in hypocalcaemic (28.3 per cent) compared with normocalcaemic (7.5 per cent) patients (p < 0.05)[31].

Ruiz Magro *et al* analyzed the incidence of metabolic disturbances in critically ill children and evaluated their correlation with severity of illness, complications, mortality and length of hospital stay in 360 Children Admitted Into A Pediatric

Intensive Care Unit (PICU). The incidence of different metabolic disturbances at admission to the PICU was: hyperglycemia 51.9%, hypoglycemia 1.9%, hypocalcemia 24.5%, hypercalcemia 5.8%, hyperphosphatemia 7.3%, hypophosphatemia 7.9%, hypomagnesemia 47.4% and hypermagnesemia 3%. Patients with shock had lower concentrations of calcium and higher phosphorus levels, while children with sepsis had lower magnesium concentrations. They concluded that metabolic disturbances in critically ill children were frequent findings, correlate with important complications and can be prognostic markers[32].

Martin *et al* studied the correlation between HCO_3 and Base deficit at admission and during the ICU stay and the predictive value of serum HCO_3 for significant metabolic acidosis and ICU mortality. Serum HCO_3 levels showed significant correlation with arterial BD levels both at admission and reliably predicted the presence of significant metabolic acidosis (BD > 5). The admission serum HCO_3 level predicted ICU mortality as accurately as the admission arterial BD (AUCs of 0.68 and 0.70, respectively) and more accurately than either admission pH or anion gap. They concluded that serum HCO_3 provides equivalent information to the arterial BD and may be used as an alternative predictive marker or guide to resuscitation. Low HCO_3 levels should prompt immediate metabolic acidosis evaluation and management[33].

A review of literature was conducted by Khilnani *et al* analyzing all published articles about electrolyte abnormalities in critically ill children over the past 20 years was reviewed and concluded that electrolyte abnormalities were common in critically ill children and can easily be treated once recognized. The author also emphasized that further studies are needed to understand the role of ionized calcium and magnesium in neonatal and pediatric critical illness[34].

STUDY JUSTIFICATION

Electrolyte disturbances are commonly encountered in a PICU. Most of the electrolyte disturbances share the clinical features with underlying illness. They either may be a primary problem or a secondary co-morbid condition. Unless anticipated, they are often over- looked and missed. Moreover early recognition and appropriate correction exerts a positive influence over the outcome. Unidentified or uncorrected dyselectrolytemias definitely contribute to increase the morbidity and mortality.

AIM OF THE STUDY

To study

(a) The pattern of electrolyte disturbances and

(b) Their impact on outcome among children treated in Paediatric Intensive Care Unit of a tertiary care hospital.

SUBJECTS AND METHODS

METHODOLOGY

Study design

Descriptive Study

Study place

Paediatric Intensive Care Unit, Institute of Child Health and Hospital for Children, Egmore, Chennai.

Study period

January 2006 to December 2006

Study population

All children in the age group 1 month to 12 years who were admitted in PICU in the above study period were included.

MANEUVER

900 children admitted in PICU in the study period were included in the study. After initial stabilization, the cases were routinely monitored for serum electrolytes and further monitoring was done on clinical necessity. Electrolyte disturbances involving

Sodium, Potassium, Calcium and Bicarbonates were identified and treated appropriately as per our hospital protocol. Age, Sex distribution, clinical features, underlying Illness, dyselectrolytemias, predisposing factors, duration of hospital stay and outcome were recorded.

Case Definitions

Hyponatremia < 135 mEq / L

Hypernatremia > 145 mEq/ L

Hypokalemia < 3.5 mEq/L

Hyperkalemia > 5.0 mEq /L (>1 year)

> 6.0 mEq/L (<1 year)

Hypocalcemia < 8.8 mg/dl (total) < 1.12 mmol/L (ionized)

Hypercalcemia >10.8 mg/dl(total) > 1.23 mmol/L (ionized)

Metabolic acidosis- serum HCO3 < 20 mEq/L

Metabolic alkalosis- serum HCO3> 28 mEq/L

} Substantiated with ABG

Abnormal values from analyzer are counter checked with central laboratory

values for confirmation serum Sodium and Potassium were estimated by Flame photometer. Bicarbonate was estimated by acid titration method. Calcium was estimated by auto analyzer. ECG was taken in cases with hypokalemia, hyperkalemia and hypocalcemia.

STATISTICAL ANALYSIS

Descriptive statistics used were frequencies and percentages. Association between electrolyte disturbances and the outcome was determined using the chi-square test (p value < 0.05 was considered as statistically significant). Univariate logistic regression of the electrolyte disturbances on the outcome variables was done. Multiple logistic regression was done to adjust for the confounding effect of other risk factors over electrolyte disturbances on the outcome.

RESULTS

900 children admitted in PICU over a period of 12 months were evaluated in the study.

TABLE - 1

AGE AND SEX DISTRIBUTION OF STUDY POPULATION

Age	Male	Female	Total
	n (%)	n (%)	n (%)
1month-1 yr	237 (59.55%)	161 (40.45%)	398 (44.22%)
1-3 years	125 (58.14%)	90 (41.86%)	215 (23.89%)
4-6 years	58 (51.33%)	55 (48.67%)	113 (12.56%)
>6 years	87 (50.0%)	87 (50.0%)	174 (19.33%)
Total	507 (56.33%)	393 (43.67%)	900

In the study population, 56.33% were males and 43.67% were females. Majority of PICU admissions were less than one year of age (44.22%).

Majority of the PICU admissions were CNS illnesses (31.78%), followed by septicemia (15.89%) and respiratory illnesses (13.44%).

DYSELECTROLYTEMIAS

Among 900 children admitted in the PICU in the study period, dyselectrolytemias were observed in 547 cases (60.77%).

TABLE - 3

INCIDENCE OF ELECTROLYTE DISTURBANCES

Dyselectrolytemias	**n**	**%**
Hyponatremia	207	23.0
Hypernatremia	189	21.0
Hypokalemia	333	37.0
Hyperkalemia	54	6.0
Metabolic acidosis	324	36.0
Hypocalcemia	279	31.0
Hypercalcemia	17	1.88

Total number of cases studied = 900.

Hypokalemia, the commonest electrolyte disturbance, was seen in 333 cases(37%) closely followed by metabolic acidosis in 324 cases(36%). Hypocalcemia was third common, seen in 279(31%) cases, followed by hyponatremia and hypernatremia. No cases with primary metabolic alkalosis were observed. More than one electrolyte disturbance was observed in most of the cases (Fig.4).

HYPONATREMIA

Hyponatremia was seen in 207 children among 900 studied. (23%)

TABLE - 4

AGE AND SEX DISTRIBUTION OF HYPONATREMIA

Age	Male		Female		Total	
	n	%	n	%		
1 month- 1year	37	(56.92%)	28	(43.08%)	65	(31.40%)
1-3 years	26	(42.62%)	35	(57.38%)	61	(29.47%)
4-6 years	17	(62.96%)	10	(37.04%)	27	(13.04%)
>6 years	37	(68.52%)	17	(31.48%)	54	(26.09%)
Total	117	(56.52%)	90	(43.48%)	207	

Among children with hyponatremia about 60% of cases were < 3 years of age. Slightly male preponderance was seen. (p value = 0.95)

Common underlying illnesses in children with hyponatremia were CNS illnesses (status epilepticus 37.83%, meningoencephalitis 35.13%, acute encephalopathy27.02%), RS illnesses (pneumonia 66.66%) and DKA. Among renal illnesses, DSS and hepatic encephalopathy nearly one-third of cases in each category had hyponatremia. (Table 5)

TABLE - 6

OUTCOME IN HYPONATREMIA

	n	No. of poor outcome	%
Hyponatremia	207	134*	64.73%
Normonatremia	504	198	39.28%

* poor outcome- 120 deaths, 14 AMA

TABLE - 7

CHI SQUARE TEST- OUTCOME IN HYPONATREMIA

	Outcome				**p-value**
	Good outcome		**Poor outcome**		
	n	**%**	**n**	**%**	
Normonatremia	306	60.7	198	39.3	0.00
Hyponatremia	73	35.3	134	64.7	

Out of 207 children with hyponatremia, 134 (64.73%) children had poor outcome

whereas it was only 39.28% among children with normal serum sodium levels, the difference observed was statistically significant. (p = 0.00)

TABLE - 8

GRADES OF HYPONATREMIA AND ASSOCIATION WITH OUTCOME

mEq/L	Number of cases	Poor outcome
131-134	90 (43.48%)	56 (62.22%)
126-130	103 (49.76%)	68 (66.01%)
< =125	14 (6.76%)	10 (71.42%)
Total	207	134 (64.73%)

Majority of cases fall under moderate hyponatremia. Proportion of cases with poor outcome was higher in children with severe hyponatremia (<= 125 mEq/ L). Increasing rate of poor outcome with decreasing serum sodium levels was not statistically significant by chi-square analysis (Fig.5).

In the studied population, among children with poor outcome, 40.36% had hyponatremia and 19.26% among those who recovered. Hyponatremia was found to be 2.8 times more among those with poor outcome when compared to those who recovered [OR (95%CI) = 2.8 (2.0- 4.0)]. In children with poor outcome, the odds of finding low GCS, assisted ventilation, shock and positive blood culture were significantly higher in children with hyponatremia. (Table 9).

TABLE - 10
RISK FACTORS FOR POOR OUTCOME AMONG CHILDREN WITH HYPONATREMIA - MULTIVARIATE ANALYSIS

Risk factors	O.R.	95% C.I.	p-value
Hyponatremia			
Yes	3.1	2.1 , 4.6	0.00
No	1.0	Reference	
Assisted ventilation			
Yes	4.0	2.6 , 6.1	0.00
No	1.0	Reference	
Shock			
Yes	2.6	1.8 , 3.8	0.00
No	1.0	Reference	

In the studied population, after adjusting for confounding effect by multiple logistic regression analysis, hyponatremia, assisted ventilation and shock were found to be independently associated with poor outcome. (Table 10)

HYPERNATREMIA

Hypernatremia was seen in 189 cases (21%)

TABLE - 11

AGE AND SEX DISTRIBUTION OF HYPERNATREMIA

Age	Male		Female		Total	
	n	%	n	%		
1 mon - 1 year	62	(62.0%)	38	(38.0%)	100	(52.91%)
1-3 years	25	(56.82%)	19	(43.18%)	44	(23.28%)
4-6 years	9	(47.37%)	10	(52.63%)	19	(10.05%)
>6 years	16	(61.54%)	10	(38.46%)	26	(13.76%)
Total	112	(59.26%)	77	(40.74%)	189	

About 75% of cases were less than 3 years of age. Male children outnumber females in the group with hypernatremia, but the association was not statistically significant (p value = 0.36).

Major underlying illnesses in children with hypernatremia were CNS illnesses (status epilepticus 37.64%, acute encephalopathy 32.94%, meningoencephalitis 29.41%), septicemia and respiratory illnesses. About one fourth of hematological cases and DSS predisposed to hypernatremia. (Table 12)

TABLE - 13

OUTCOME IN CHILDREN WITH HYPERNATREMIA

	n	**No. of poor outcome**	**%**
Hypernatremia	189	99*	52.38%
Normonatremia	504	198	39.28%

* poor outcome – 90 deaths, 9 AMA

TABLE - 14

CHI SQUARE TEST- OUTCOME IN HYPERNATREMIA

	Outcome				**p-value**
	Good outcome		**Poor outcome**		
	n	**%**	**n**	**%**	
Normonatremia	306	60.7	198	39.3	0.003
Hypernatremia	90	47.6	99	52.4	

Compared to children with normal serum sodium levels, presence of hypernatremia was significantly associated with poor outcome.

In the studied population, among children with poor outcome, 33.33% had

hypernatremia and 22.73% among those who recovered. Hypernatremia was found to be 1.7 times more among those with poor outcome when compared to those who recovered [OR (95%CI) = 1.7 (1.2- 2.4)]. In children with poor outcome, the odds of finding age of 3 years and less, assisted ventilation, shock bleeding manifestations, renal failure and positive blood culture were significantly higher in children with hypernatremia. (Table 15)

TABLE - 16

RISK FACTORS FOR POOR OUTCOME AMONG CHILDREN WITH HYPERNATREMIA - MULTIVARIATE ANALYSIS

Risk factors	O.R.	95% C.I.	p-value
Hypernatremia			
Yes	1.9	1.4 , 2.7	0.00
No	1.0	Reference	
Age in years			
<=3	2.1	1.3 , 3.5	0.00
>3	1.0	Reference	

In the study population, after adjusting for the confounding effect by multiple logistic regression analysis, hypernatremia and age of 3 years and less were found to be independent risk factors for poor outcome (Table 16).

HYPOKALEMIA

Hypokalemia was seen in 333 cases out of 900 studied. (37%)

TABLE - 17

AGE AND SEX DISTRIBUTION OF HYPOKALEMIA

Age	Male		Female		Total
	n	%	n	%	
1 mon- 1 year	70	(59.32%)	48	(40.68%)	118 (35.44%)
1-3 years	53	(53.54%)	46	(46.46%)	99 (29.73%)
3-6 years	33	(75.0%)	11	(25.0%)	44 (13.21%)
>6 years	34	(47.22%)	38	(52.78%)	72 (21.62%)
Total	190	(57.06%)	143	(42.94%)	333

Nearly two-thirds of cases with hypokalemia were under 3 years of age. Slight male predominance was seen, but it was not statistically significant (p value 0.74).

Hypokalemia was commonly seen in children with underlying neurological illnesses (meningoencephalitis 37.58%, status epilepticus 32.21%, acute

encephalopathy30.20%) ,septicemia and respiratory illnesses. Nearly one-half of the cases with DKA manifested hypokalemia. (Table 18)

TABLE - 19

OUTCOME IN CHILDREN WITH HYPOKALEMIA

	n	**No. of poor outcome**	**%**
Hypokalemia	333	162*	48.65%
Normokalemia	513	233	45.42%

* poor outcome – 145 deaths, 17 AMA

TABLE - 20

CHI SQUARE TEST- OUTCOME IN HYPOKALEMIA

	Outcome				**p-value**
	Good outcome		**Poor outcome**		
	n	**%**	**n**	**%**	
Normokalemia	280	54.6	233	45.4	0.36
Hypokalemia	171	51.4	162	48.6	

Children with hypokalemia showed increased poor outcome, but the association was not statistically significant. (p value= 0.36)

In the studied population, among children with poor outcome, 41.01% had

hypokalemia and 37% .92% among those who recovered. Hypokalemia was found to be 1.1 times more among those with poor outcome when compared to those who recovered [OR (95%CI) = 1.1 (0.9- 1.5)].(p value 0.36)

TABLE - 22

GRADES OF HYPOKALEMIA AND ASSOCIATION WITH OUTCOME

Grade (mEq/L)	Number of cases	Poor outcome
Mild (3.0-3.4)	110 (33.03%)	28 (25.45%)
Moderate (2.0-2.9)	204 (61.26%)	120 (58.54%)
Severe (<2)	19 (5.71%)	14 (73.68%)
Total	333	162 (48.64%)

(p value =0.00), by chi-square analysis for trend

With decreasing serum potassium levels, there was an increase in poor outcome and the association was found to be statistically significant. ECG changes correlated poorly with serum potassium levels (Fig.6).

HYPERKALEMIA

Hyperkalemia was seen in 54 children (6.0%)

TABLE - 23

AGE AND SEX DISTRIBUTION OF HYPERKALEMIA

Age	Male		Female		Total
	n	%	n	%	
1mon- 1 year	10	(52.63%)	9	(47.37%)	19 (35.19%)
1-3 years	8	(66.67%)	4	(33.33%)	12 (22.22%)
3-6 years	7	(53.85%)	6	(46.15%)	13 (24.07%)
>6 years	2	(20.0%)	8	(80.0%)	10 (18.52%)
Total	27	(50.0%)	27	(50.0%)	54

More than half of the cases were under 3 years of age. Both males and females were equally affected.

Major underlying illnesses in children with hyperkalemia were CNS illnesses followed by renal illnesses and septicemia. (Table 24)

TABLE - 25

OUTCOME IN CHILDREN WITH HYPERKALEMIA

	n	No. of poor outcome	%
Hyperkalemia	54	36*	66.67%
Normokalemia	513	233	45.42%

* poor outcome – 32 deaths, 4 AMA

TABLE - 26

CHI SQUARE TEST- OUTCOME IN HYPERKALEMIA

	Outcome				p-value
	Good outcome		Poor outcome		
	n	%	n	%	
Normokalemia	280	54.6	233	45.4	0.004
Hyperkalemia	18	33.3	36	66.7	

Children with hyperkalemia showed increased rate of poor outcome as compared to children with normal serum potassium levels. Presence of hyperkalemia was found to significantly associated with poor outcome. (p 0.004). ECG changes were seen infrequently.

In the studied population, among children with poor outcome, 13.38% had

hyperkalemia and 6.04% among those who recovered. Hyperkalemia was found to be 2.4 times more among those with poor outcome when compared to those who recovered [OR (95%CI) = 2.4 (1.3- 4.3)]. In children with poor outcome, the odds of finding assisted ventilation, shock, renal failure and positive blood culture were significantly higher in children with hyperkalemia. (Table 27)

TABLE - 28

RISK FACTORS FOR POOR OUTCOME AMONG CHILDREN WITH HYPERKALEMIA - MULTIVARIATE ANALYSIS

Risk factors	O.R.	95% C.I.	p-value
Hyperkalemia			
Yes	1.9	1.0 , 3.9	0.06
No	1.0	Reference	
Assisted ventilation			
Yes	9.1	5.6 , 14.9	0.00
No	1.0	Reference	
Shock			
Yes	1.7	1.2 , 2.6	0.008
No	1.0	Reference	

In the study population, hyperkalemia was not found to be an independent risk factor for poor outcome (Table 28).

HYPOCALCEMIA

Hypocalcemia was seen in 279 cases (31.0%) out of 900 studied.

TABLE - 29

AGE AND SEX DISTRIBUTION OF HYPOCALCEMIA

Age	Male		Female		Total
	n	%	n	%	
1mon- 1 year	73	(50.0%)	73	(50.0%)	146 (52.34%)
1-3 years	44	(72.13%)	17	(27.87%)	61 (21.86%)
4-6 years	20	(66.67%)	10	(33.33%)	30 (10.75%)
>6 years	25	(59.52%)	17	(40.48%)	42 (15.05%)
Total	162	(58.06%)	117	(41.94%)	279

Hypocalcemia was commonly seen among infants (52.32%). Male preponderance was seen but statistically not significant (p value =0.48).

Most common underlying illnesses were CNS illnesses (status epilepticus 39.17%, meningoencephalitis 36.08%, acute encephalopathy 24.74%), septicemia and respiratory illnesses. Nearly half of the cases with renal illnesses manifested hypocalcemia. (Table 30)

TABLE - 31

OUTCOME IN CHILDREN WITH HYPOCALCEMIA

	n	No. of poor outcome	%
Hypocalcemia	279	153*	54.84%
Normocalcemia	603	278	46.10%

* poor outcome – 139 deaths, 14 AMA

TABLE - 32

CHI SQUARE TEST- OUTCOME IN HYPOCALCEMIA

	Outcome				p-value
	Good outcome		Poor outcome		
	n	%	n	%	
Normocalcemia	325	53.9	278	46.1	0.02
Hypocalcemia	126	45.2	153	54.8	

Children with low serum calcium levels had increased rate of poor outcome as compared to children with normal calcium levels. The association was found to be statistically significant (p value = 0.02).

In the studied population, among children with poor outcome, 35.49% had hypocalcemia and 27.94% among those who recovered. Hypocalemia was found to be 3.0 times more among those with poor outcome when compared to those who recovered [OR (95%CI) = 3.0 (2.2- 4.0)]. In children with poor outcome the frequency of finding

age of 3 years and less, low GCS, assisted ventilation, shock and positive blood culture were significantly higher in children with hypocalcemia. (Table 33)

TABLE - 34

RISK FACTORS FOR POOR OUTCOME AMONG CHILDREN WITH HYPOCALCEMIA - MULTIVARIATE ANALYSIS

Risk factors	O.R.	95% C.I.	p-value
Hypocalcemia			
Yes	1.4	1.1 , 1.9	0.02
No	1.0	Reference	
NEC			
Growth	1.5	1.1 , 2.1	0.01
No growth	1.0	Reference	

In the study population, after adjusting for the confounding effect by multiple logistic regression analysis, hypocalcemia and blood culture positivity were found to be independent risk factors for poor outcome. (Table 34).

HYPERCALCEMIA

Hypercalcemia was seen in 17 cases out of 900. (1.88%)

TABLE - 35

AGE AND SEX DISTRIBUTION OF HYPERCALCEMIA

Age	Male		Female		Total	
	n	%	n	%		
1 mon- 1 year	-		-		-	
1-3 years	1	(50.0%)	1	(50.0%)	2	(11.76%)
4-6 years	1	(50.0%)	1	(50.0%)	2	(11.76%)
>6 years	11	(84.62%)	2	(15.38%)	13	(76.48%)
Total	13	(76.47%)	4	(23.53%)	17	

Nearly three-fourths of the children with hypercalcemia were more than 6 years of age. Males outnumbered females but the difference was not statistically significant. (p value = 0.09)

Most common underlying illnesses were RS illnesses, CNS illnesses and septicemia. (Table 36)

TABLE - 37

OUTCOME IN CHILDREN WITH HYPERCALCEMIA

	n	**No. of poor outcome**	**%**
Hypercalcemia	17	-	-
Normocalcemia	603	278	46.10%

All 17 children with hypercalcemia showed good outcome.

METABOLIC ACIDOSIS

Metabolic acidosis was observed in 324 children (36.0%).

TABLE - 38

AGE AND SEX DISTRIBUTION OF METABOLIC ACIDOSIS

Age	Male		Female		Total
	n	%	n	%	
1mon- 1 year	56	(44.09%)	71	(55.91%)	127 (39.20%)
1-3 years	34	(61.82%)	21	(38.18%)	55 (16.98%)
4-6 years	27	(52.94%)	24	(47.06%)	51 (15.74%)
>6 years	48	(52.75%)	43	(47.25%)	91 (28.08%)
Total	165	(50.93%)	159	(49.07%)	324

Majority of children with metabolic acidosis were found to be less than 3 years of age (56.17%). Slightly male predominance was seen, which was found to be statistically significant (p value = 0.01).

Metabolic acidosis was commonly observed in children with CNS illnesses

(meningoencephalitis 46.60%, acute encephalopathy31.07%, status epilepticus 22.33%), septicemia and respiratory illnesses. 85.36% of children with DKA manifested metabolic acidosis. (Table 39)

TABLE - 40
OUTCOME IN CHILDREN WITH METABOLIC ACIDOSIS

Metabolic acidosis	n	No. of poor outcome	%
Yes	324	171*	52.77%
No	576	260	45.14%

* poor outcome – 156 deaths, 15 AMA

TABLE - 41
CHI SQUARE TEST- OUTCOME IN METABOLIC ACIDOSIS

Metabolic Acidosis	Outcome				p-value
	Good outcome		Poor outcome		
	n	%	n	%	
Yes	153	47.2	171	52.8	0.03
No	316	54.9	260	45.1	

Children with metabolic acidosis showed increased rate of poor outcome and the association was found to be statistically significant. (p value 0.03)

In the studied population, among children with poor outcome, 39.68% had metabolic acidosis and 32.62% among those who recovered. Metabolic acidosis was

found to be 1.4 times more among those with poor outcome when compared to those who recovered [OR (95%CI) = 1.4 (1.0- 1.8)]. In children with poor outcome the frequency of finding age of 3 years and less, low GCS, assisted ventilation, shock, hypoglycemia and positive blood culture were significantly higher in children with metabolic acidosis. (Table 42)

TABLE - 43

RISK FACTORS FOR POOR OUTCOME AMONG CHILDREN WITH METABOLIC ACIDOSIS - MULTIVARIATE ANALYSIS

Risk factors	O.R.	95% C.I.	p-value
Acidosis			
Yes	1.4	1.0 , 1.9	0.03
No	1.0	Reference	
Age in years			
<=3	2.4	1.6 , 3.8	0.00
>3	1.0	Reference	
Hypoglycemia			
Yes	1.7	1.1 , 2.7	0.01
No	1.0	Reference	

In the study population, metabolic acidosis, age of 3 years and less and hypoglycemia were found to be independently associated with poor outcome. (Table 43)

COMBINED DYSELECTROLYTEMIAS

Since disturbances involving 4 electrolytes were studied, combined dyselectrolytemias were commonly observed. Among 547 children with dyselectrolytemias, 430 (78.61%) had more than one electrolyte disturbances.

Commonest combination observed was hypokalemia with metabolic acidosis.

TABLE - 44

COMBINED DYSELECTROLYEMIAS

Combined dyselectrolytemias	Number of cases	Percentage of total study population (n =900)
Hypokalemia + metabolic acidosis	164	18.22%
Hypokalemia + hypocalcemia	92	10.22%
Hypokalemia + hyponatremia	85	9.44%

More than 2 electrolyte disturbances were seen in 113 children (26.74%). Disturbances involving all 4 electrolytes were seen in 5 cases (1.1%).

TABLE - 46

OUTCOME ANALYSIS IN DYSELECTROLYTEMIAS

Dyselectrolytemias	Outcome				p-value
	Good outcome		Poor outcome		
	n	%	n	%	
Yes	237	43.33	310	56.67	0.0001
No	234	66.29	119	37.71	

The increased rate of poor outcome in children with dyselectrolytemias was found to be statistically significant.

TABLE - 47

OUTCOME ANALYSIS IN MULTIPLE DYSELECTROLYTEMIAS

More than one electrolyte disturbances	Outcome				p-value
	Good outcome		Poor outcome		
	n	%	n	%	
Yes	166	38.60	264	61.40	0.0001
No	71	60.68	46	39.32	

Children with more than one electrolyte disturbance had increased rate poor outcome which was statistically significant.

DISCUSSION

In this study, dyslectrolytemias were observed in 60.77% of PICU admissions in contrast to the study by Subba Rao *et al*[20] which showed the incidence of elecytrolyte disturbances to be 32.4%.This difference could be accounted for the fact that only disturbances of sodium and potassium were studied by Subba Rao *et al*. Also in their study hyponatremia and hypernatremia were defined as <130 mEq/L and > 150 mEq/L respectively. In this study hyponatremia and hypernatremia were defined as <135 mEq/L and > 145 mEq/L respectively[2].

HYPOKALEMIA

Hypokalemia was the commonest electrolyte disturbance seen in children admitted to PICU in our set up. Hypokalemia was seen in 37% of cases. These findings were in contrast to those by Subba Rao *et al*[20], who found hyperkalemia as the commonest electrolyte disturbance among PICU admissions. The frequency of hypokalemia in this study was higher as compared to a retrospective study by Singhi *et al*[21], which showed hypokalemia in only 14.8% of cases. The common underlying illnesses in cases with hypokalemia in this study were CNS illnesses (44.75%), septicemia (13.81%) and respiratory illnesses (11.71%). The predisposing factors for increased frequency of hypokalemia in this study can be explained by

1. Underlying illness by itself.

2. CNS illnesses predispose to hypokalemia by several factors- poor oral intake prior to admission, presence of vomiting, usage of drugs like mannitol and corticosteroids[14] and stress induced catecholamine release[21, 35].

3. Use of medications like diuretics (in cardiac and renal illnesses), beta agonists (in asthma) and insulin (in DKA).

4. Pre existing malnutrition- decreased body potassium stores[11].

5. Inappropriately high circulating ADH levels in children with meningoencephalitis and pneumonia[36, 37, 38, 39].

The CNS illnesses being the common underlying disease can be partly accounted by the fact that they constitute 31.18% (286 cases) of the PICU admissions in this study as compared to 17.9% (169 cases) in a prospective study done by Khilnani *et al* in New Delhi[40]. In this study majority of cases 74.07% of hypokalemia fell under moderate category in similar to the study by Singhi *et al*[21] which showed majority (68.6%) of hypokalemic episodes were moderate. The overall rate of poor outcome in cases with hypokalemia was 48.6% which was higher as compared to 25.6% mortality in the study by Singhi *et al*[21]. This higher rate poor of outcome can be accounted for by the nature of underlying illnesses. The severity of the disturbance correlated with increased risk of poor outcome which was similar to the study by Singhi *et al*[22].

METABOLIC ACIDOSIS

Metabolic acidosis, low serum bicarbonate levels supported by ABG analysis, was the second common electrolyte disturbance observed (36%). Nearly one third of cases were seen in children less than one year of age which may be accounted by the relative immaturity of the renal system in handling acid base disturbances. Conditions resulting in hypoxia, respiratory failure and perfusion abnormalities predisposed to metabolic acidosis, the common underlying illnesses being CNS illnesses (31.79%), Septicemia (20%) and RS illnesses (13.89%). Though outcome depends mainly on the nature of underlying illnesses, metabolic acidosis was found to be an independent risk factor for poor outcome by multivariate analysis. In studies by Martin *et al*[33] and Eachempati *et al*[41], it has been shown that serum bicarbonate levels correlate well arterial base deficit in critically ill patients.

HYPOCALCEMIA

Hypocalcemia was found to be the third common electrolyte disturbance observed in 31% of cases. The incidence of hypocalcemia was higher as compared to the study by Ruiz Magro *et al*[32], Madrid in which the incidence of ionized hypocalcemia was stated as 24.5%. Infants commonly manifested hypocalcemia. The rate of poor outcome in children with ionized hypocalcemia was 54.8% which was higher as compared to 31%

by Cardenas-Rivero *et al*[30] and 28.3% by Singhi et *al*[31]. This higher rate of poor outcome may be accounted by the underlying illnesses. In children with poor outcome, the odds of finding low GCS, on assisted ventilation, shock and sepsis were significantly more in children with hypocalcemia. Cardenas-Rivero *et al* also had demonstrated that more children with ionized hypocalcemia had sepsis (p =0.0299)[30]. Hypocalcemia was found to be an independent risk factor for poor outcome in similar to various studies[30, 31].

HYPONATREMIA

Hyponatremia was seen in 23% of cases which was lower as compared to 29.8% of cases in a prospective study done by Prasad *et al*[24]. The lower incidence in this study can be accounted by that diarrheal illnesses were not included in this study. But the incidence of severe hyponatremia (serum sodium =< 125 mEq/L) was 6.7% similar to 6.4% in the study by Prasad *et al*[24]. The frequency of hyponatremia in RS illnesses was 24.79% which was similar to Prasad *et al*'s observation of 26% in children with pneumonia[24]. 35.75% of children with hyponatremia had underlying neurological illnesses which was higher in comparison to 10.8% as showed by Pizzotti *et al*[42]. Role of inappropriately higher concentration of ADH has been demonstrated in association with euvolemic hyponatremia in children with meningitis[43, 44, 45]. Intracellular shift of sodium and water in septicemia has been demonstrated in various studies[46,47]. In this study the rate of poor outcome in children with hyponatremia was 64.7%. Hyponatremia was found to be an independent risk factor for poor outcome as compared to children with

normal serum sodium levels and it can be considered as a poor prognostic marker[27], though increased mortality was mainly attributed to the progression of underlying disease[48]. Arieff *et al* have reported the mortality rate in hyponatremia to be as high as 50% in adults[49].

HYPERNATREMIA

Hypernatremia was found in 21% of cases among whom nearly half of them were infants. Sick infants were entirely dependent on caregivers for access to water and were more prone to develop hypernatremia. 44.97% of children had underlying CNS illnesses which was higher as compared to the study by Moritz *et al*[28] which showed underlying neurological impairment in 38% of cases. In addition to the dependency on caregivers for the fluid requirement, a CNS lesion affecting the thirst centre increases their susceptibility for developing hypernatremia[8, 48]. In this study, The rate of poor outcome in cases with hypernatremia was 52.4% almost similar to 48% mortality rate in hypernatremic patients showed by Howanitz *et al*[50]. Apart from the progression of underlying disesase, hypernatremia was found to be an independent risk factor for poor outcome. This was in contrast to a study in adults by Aiyagari *et al* which showed that only severe hypernatremia (serum sodium >160 mEq/L) was independently associated with increased mortality[29]. Role of mannitol[8] and 3% hypertonic saline in predisposing to hypernatremia needs further evaluation.

HYPERKALEMIA

Hyperkalemia was found in 6.0% of PICU admissions which was similar to a prospective study by Singhi *et al*[22] which showed hyperkalemia in 5.4% cases. Among children with hyperkalemia 42.59% had an underlying CNS illness which was in contrast to the studies by Subba rao *et al*[20] and Singhi *et al*[22]. In this study, the rate of poor outcome in hyperkalemic children was 66.7% in contrast to 22.7% as shown by Subba Rao *et al*[20]. The increased incidence of poor outcome may be accounted by the pattern of underlying illnesses. Hyperkalemia was found to worsen the outcome in the presence of assisted ventilation, shock, sepsis and renal failure.

HYPERCALCEMIA

Hypercalcemia was found in 1.88% of children in this study in contrast to the retrospective study by Ruiz Magro *et al* which showed 5.8% incidence of hypercalcemia in critically ill children[32]. Hypercalcemia was commonly seen in older children and none of the children with hypercalcemia showed poor outcome.

Combined dyselectrolytemias were commonly observed. The commonest combination was hypokalemia with metabolic acidosis. Presence of hypokalemia in the context of metabolic acidosis signifies the magnitude of depletion of total body potassium stores. Children with combined electrolyte disturbances had higher rate of poor outcome, similar to observations made by Subba Rao *et al*[20] and Singhi *et al*[22, 27].

Presence of combined dyselectrolytemias underscores the severity of the underlying illnesses affecting the internal homeostasis.

Certain limitations do exist in this study. Serum osmolality was estimated in many cases rather than being measured. Urine osmolality and urine electrolytes would have thrown light on urinary losses of electrolytes, helping us in better understanding of the etiopathogenesis of dyselectrolytemias. Inclusion of serum magnesium would have enhanced the value of the study. In view of heterogenous group of study population and individual variability, the influence of underlying illnesses on outcome, which plays a major and significant role, was not quantified.

SUMMARY

* Electrolyte disturbances were observed in 60.77% of PICU admissions.
* Hypokalemia was the commonest electrolyte disturbance observed in 37% of cases.
* Metabolic acidosis was seen in 36% of cases and hypocalcemia in 31% of PICU admissions.
* Hyponatremia was observed in 23% and hypernatremia in 21% of patients.
* Hyperkalemia was seen in 6.0% of cases.
* Hypercalcemia was seen only in 1.88% cases.
* Metabolic alkalosis was not observed.
* Combined dyselectrolytemias were observed in 430 cases (78.61%), the commonest combination being hypokalemia with metabolic acidosis.
* CNS illnesses were the common underlying illnesses for most dyselectrolytemias.
* Hypokalemia was associated with high rate of poor outcome, which increased significantly with the severity of hypokalemia.
* Hyperkalemia was associated with high poor outcome rate of 66.7%.
* Metabolic acidosis, hypocalcemia, hyponatremia and hypernatremia were found to be independently associated with poor outcome.

* In cases with metabolic acidosis, age of 3 years and less and hypoglycemia were found to be independent risk factors for poor outcome.

* In children with hypocalcemia, blood culture positivity was an independent risk factor for poor outcome.

* In hyponatremic children, need for assisted ventilation and presence of shock were found to be independently associated with poor outcome.

* In cases with hypernatremia, age of 3 years and less was independently associated with poor outcome.

* Combined dyselectrolytemias carried significantly higher risk of poor outcome.

CONCLUSION

* Electrolyte disturbances are commonly encountered in PICU.

* Dyselectrolytemias significantly influence the outcome, despite multiple determining factors.

- High index of suspicion, early recognition and timely interventions to correct the electrolyte disturbances are mandatory.

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ANNEXURE
PROFORMA

ELECTROLYTE IMBALANCES IN PICU,ICH&HC

NAME: **AGE:** **M/F** **Wt:** **SERIAL NO:**

DATE&TIME OF ADMN.TO IMCU: **PICU NO:** **I.P NO:**

OUTCOME: IMP / EXP / AMA **DURATION OF STAY IN PICU:**

SYMPTOMS:

fits	**palpitation**	**abd.distension**
ALOC	**breathlessness**	**polyuria**
Muscle twitching	**vomiting /dur**	**polydypsia**
Carpopedalspasm	**&freq**	**edema**
Flaccid weakness	**loose stools/**	**oliguria**
Headache	**dur&freq**	**lethargy**
Develop.delay	**fever**	**skeletal abn.**
ORS	**FTT**	**formula feeds**
H/o chronic illness		

SIGNS:

AirwayS/U/I							
R.R/min							
W.O.B↑/N/↓							
T.V. ↑/N/↓							
B.A.E ⇔/≠							
Addedsounds							
Uppera.w.obst							
S1 S2							
Murmur							
H.R./min							
perfusion							
SaO2							
B.P.mm Hg							
Liver span							
HydrationA/E/D							
TEMP.degF							
A/V/P/U							
GCS							
Fits +/−							
ALOC							

DEM PUPIL Tone/Posture Fundus							

INVESTIGATIONS:

Bld.sugar							
Na+ meq/L							
K+ meq/L							
HCO3meq/L							
Ca(T)mg/dl							
Ca(I)mmol/L							
ABG							
Others	**Hb** **NEC**		**Urea** **Creatinine**		**CXR**		
I **N** **T** **E** **R** **V** **ENTIONS**							

DIAGNOSIS: